

Inventors: John C. Reed
Serial No.: 09/388,221
Filed: September 1, 1999
Page 2

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wherein said polypeptide comprises an NB-ARC domain capable of associating with the NB-ARC domain of SEQ ID NO:2,

wherein said polypeptide does not comprise amino acids 957-987 of SEQ ID NO:2, and

wherein said polypeptide associates with SEQ ID NO:2 or with Apaf-1.

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4. (Amended) An isolated nucleic acid molecule encoding a NB-ARC and CARD containing protein (NAC), comprising a nucleotide sequence set forth in either of SEQ ID NOs:3 or 5.

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8. (Three Times Amended) An oligonucleotide consisting of at least 500 contiguous nucleotides up to 1035 contiguous nucleotides of the nucleotide sequence set forth in any of SEQ ID Nos: 1, 3 and 5 or the complement of said nucleotide sequence, and a nucleotide sequence at the 5' or 3' end that differs from the nucleotide sequence set forth in any of SEQ ID Nos: 1, 3 and 5 or the complement of said nucleotide sequence.

27. (Twice Amended) A method for identifying a nucleic acid molecule encoding a mammalian NAC, said method comprising:

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contacting a sample containing nucleic acid molecules with the oligonucleotide of any one of claims 77, 78, 79, 80, 81 or 82, wherein said contacting is effected under high stringency hybridization conditions, and identifying a nucleic acid molecule that hybridizes thereto, wherein said nucleic acid molecule encodes a mammalian NAC polypeptide that associates with SEQ ID NO:2 or with Apaf-1.

Inventors: John C. Reed
Serial No.: 09/388,221
Filed: September 1, 1999
Page 3

38. (Twice Amended) A method of modulating the level of Apaf-1-mediated apoptosis in a cell *in vitro*, comprising the steps of:

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- a) introducing a nucleic acid molecule encoding a NAC according to claim 1 into the cell *in vitro*; and
 - b) expressing said NAC in said cell, wherein the expression of said NAC modulates Apaf-1-mediated apoptosis in said cell.

70. (Amended) An isolated nucleic acid molecule encoding a NB-ARC and CARD containing protein (NAC), comprising a nucleotide sequence encoding SEQ ID NO:4 or 6.

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71. (Twice Amended) An isolated nucleic acid molecule encoding a NAC, comprising a nucleotide sequence encoding a polypeptide having at least 80% identity to SEQ ID NO:2, or the complement of said nucleotide sequence,

wherein said polypeptide comprises amino acids 1262-1305 of SEQ ID NO:2,

wherein said polypeptide forms a CARD domain fold,

wherein said polypeptide comprises an NB-ARC domain capable of associating with the NB-ARC domain of SEQ ID NO:2, and

wherein said polypeptide associates with SEQ ID NO:2 or with Apaf-1.

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75. (Amended) An isolated nucleic acid molecule encoding a NB-ARC and CARD containing protein (NAC), comprising a nucleotide sequence encoding SEQ ID NO:2.

Inventors: John C. Reed
Serial No.: 09/388,221
Filed: September 1, 1999
Page 4

77. (Twice Amended) An oligonucleotide comprising a nucleotide sequence consisting of nucleotides 985-1641 of SEQ ID NO:1 or its complement, or a fragment thereof consisting of at least 500 contiguous nucleotides therefrom, and a nucleotide sequence at the 5' or 3' end that differs from SEQ ID NO:1 or its complement.

78. (Twice Amended) An oligonucleotide comprising a nucleotide sequence consisting of nucleotides 2422-2844 of SEQ ID NO:1 or its complement, and a nucleotide sequence at the 5' or 3' end that differs from SEQ ID NO:1 or its complement.

79. (Twice Amended) An oligonucleotide comprising a nucleotide sequence consisting of nucleotides 3235-3960 of SEQ ID NO:1 or its complement, and a nucleotide sequence at the 5' or 3' end that differs from SEQ ID NO:1 or its complement.

80. (Twice Amended) An oligonucleotide comprising a nucleotide sequence consisting of nucleotides 2870-2959 of SEQ ID NO:1 or its complement, and a nucleotide sequence at the 5' or 3' end that differs from SEQ ID NO:1 or its complement.

81. (Twice Amended) An oligonucleotide comprising a nucleotide sequence consisting of nucleotides 4117-4419 of SEQ ID NO:1 or its complement, and a nucleotide sequence at the 5' or 3' end that differs from SEQ ID NO:1 or its complement.

Inventors: John C. Reed
Serial No.: 09/388,221
Filed: September 1, 1999
Page 5

82. (Amended) An oligonucleotide comprising at least 100 contiguous nucleotides of the nucleotide sequence set forth as nucleotides 3784-3915 of SEQ ID NO:1 or its complement.

83. (Amended) A method of modulating the level of Apaf-1-mediated apoptosis in a cell *in vitro*, comprising the steps of:

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- a) introducing a nucleic acid molecule encoding a NAC according to claim 71 into the cell *in vitro*; and
 - b) expressing said NAC in said cell, wherein the expression of said NAC modulates Apaf-1-mediated apoptosis in said cell.

84. (Amended) A method of modulating the level of Apaf-1-mediated apoptosis in a cell *in vitro*, comprising the steps of:

- a) introducing a nucleic acid molecule encoding a NAC functional fragment according to claim 66 into the cell *in vitro*; and
- b) expressing said NAC functional fragment in said cell, wherein the expression of said NAC functional fragment modulates Apaf-1-mediated apoptosis in said cell.

Inventors: John C. Reed
Serial No.: 09/388,221
Filed: September 1, 1999
Page 6

85. (Amended) A method of modulating the level of Apaf-1-mediated apoptosis in a cell *in vitro*, comprising the steps of:

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- a) introducing a nucleic acid molecule encoding a NAC functional fragment according to claim 86 into the cell *in vitro*; and
 - b) expressing said NAC functional fragment in said cell, wherein the expression of said NAC functional fragment modulates Apaf-1-mediated apoptosis in said cell.

Please add claims 89 - 104 as follows:

89. (New) The nucleic acid molecule of claim 4, wherein said nucleic acid molecule is cDNA.

90. (New) A vector containing the nucleic acid molecule of claim 89.

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91. (New) Recombinant cells containing the nucleic acid molecule of claim 4.

92. (New) A method for expression of a NAC protein, said method comprising culturing cells of claim 91 under conditions suitable for expression of said NAC.

93. (New) A method of modulating the level of Apaf-1-mediated apoptosis in a cell *in vitro*, comprising the steps of:

Inventors: John C. Reed
Serial No.: 09/388,221
Filed: September 1, 1999
Page 7

- a) introducing a nucleic acid molecule encoding a NAC according to claim 4 into the cell *in vitro*; and
- b) expressing said NAC in said cell, wherein the expression of said NAC modulates Apaf-1-mediated apoptosis in said cell.

94. (New) The nucleic acid molecule of claim 70 or 75, wherein said nucleic acid molecule is cDNA.

95. (New) A vector containing the nucleic acid molecule of claim 94.

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96. (New) Recombinant cells containing the nucleic acid molecule of claim 94.

97. (New) A method for expression of a NAC protein, said method comprising culturing cells of claim 96 under conditions suitable for expression of said NAC.

98. (New) A method of modulating the level of Apaf-1-mediated apoptosis in a cell *in vitro*, comprising the steps of:

- a) introducing a nucleic acid molecule encoding a NAC according to claim 70 or 75 into the cell *in vitro*; and
- b) expressing said NAC in said cell, wherein the expression of said NAC modulates Apaf-1-mediated apoptosis in said cell.

99. (New) A functional fragment of an isolated nucleic acid molecule encoding a NB-ARC and CARD containing

Inventors: John C. Reed
Serial No.: 09/388,221
Filed: September 1, 1999
Page 8

protein (NAC), comprising a nucleotide sequence set forth in either of SEQ ID NOs:3 or 5, wherein said functional fragment comprises a nucleotide sequence encoding a CARD domain corresponding to amino acids 1128-1261 and 1306-1473 of SEQ ID NO:2, and wherein said functional fragment associates with SEQ ID NO:2 or with Apaf-1.

100. (New) An oligonucleotide consisting of the nucleotide sequence set forth as nucleotides 985-1641 of SEQ ID NO:1 or its complement, or a fragment thereof consisting of at least 500 contiguous nucleotides therefrom.

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Cox 101. (New) An oligonucleotide consisting of the nucleotide sequence set forth as nucleotides 2422-2844 of SEQ ID NO:1 or its complement.

102. (New) An oligonucleotide consisting of the nucleotide sequence set forth as nucleotides 3235-3960 of SEQ ID NO:1 or its complement.

103. (New) An oligonucleotide consisting of the nucleotide sequence set forth as nucleotides 2870-2959 of SEQ ID NO:1 or its complement.

104. (New) An oligonucleotide consisting of the nucleotide sequence set forth as nucleotides 4117-4419 of SEQ ID NO:1 or its complement.